

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/001818

A. CLASSIFICATION OF SUBJECT MATTER IPC <sup>7</sup> A61K 31/66 C07D 311/38 C07C 15/18 C07C 39/15 A61K 31/05 A61K 31/04 A61P 39/06 C12Q 1/68 A61K 31/015 A61K 31/352 A61K 31/353 A61K 31/397 A61K 31/122 A61K 31/404 A61K 31/40 A61K 31/44 A61K 31/505 A61K 35/00		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) IPC <sup>7</sup> A61K A61P		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base, and, where practicable, search terms used) Delphion; MEDLINE; BIOSIS; CA SEARCH; SciSearch; Manual, Alternative and Natural Therapy; CAB ABSTRACTS; Derwent Biotechnology Resource; General Science Abstracts/Fulltext; Dissertation Abstracts Online; Elsevier Biobase; EMBASE; PubMed; Science; Canadian Patent Database; <i>search terms</i> : resveratrol, egr-1		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FEBS Letters, Vol. 532/3, December 2002, RAGIONE et al., "Antioxidants Induce Different Phenotypes By A Distinct Modulation of Signal Transduction", pages 289-294  *see abstract, page 292-293*	2 (part), 15 (part)
X	The Journal of Biological Chemistry, Vol. 278(26), June 27 2003, RAGIONE et al., "p21 <sup>Cip1</sup> Gene Expression Is Modulated by Egr1: A Novel Regulatory Mechanism Involved In The Resveratrol Antiproliferative Effect", pages 23360-23368.  *see abstract, page 23363-23367*	2 (part), 15 (part)
X	Life Sciences, Vol. 72(26), May 16 2003, QUINONES et al., "The Egr-1 Gene Is Induced By DNA-Damaging Agents And Non-Genotoxic Drugs In Both Normal And Neoplastic Human Cells", pages 2975-2992  *see pages 2982-2983, 2988-2989*	2 (part), 15 (part)
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international-type search 22 December 2004 (22-12-2004)		Date of mailing of the international-type search report 28 February 2005 (28-02-2005)
Name and mailing address of the ISA/ Commissioner of Patents Canadian Patent Office - PCT Ottawa/Gatineau K1A 0C9 Facsimile No. 1-819-953-9358		Authorized officer Stephanie Michaud (819) 934-2328

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/001818

Continuation of Box No. II Part 2.

Claims 1, 2 (part), 3-14, 15 (part), 16, 25-26:

Claims 1, 2 (part), 3-14, 15 (part), 16, 25-26 relate to a very large number of possible compounds, methods, egr-1 response element consensus sequences and genes. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 is to be found however solely for the compound resveratrol and specific use thereof in modulation of the egr-1 response element consensus sequence comprising AGCCCCGC for affecting the expression state of the APO A1 gene only.

In addition, claims 1, 3-14, 26 do not meet the requirements of Article 6 PCT because the subject-matter is defined in terms of the result to be achieved rather than in terms of technical features as required by Rule 6.3(a) PCT. Thus, the following expressions are considered to be functional features:

"use of a compound capable for modulating transcription arising from an egr-1 response element"; "a compound capable of modulating expression of a gene"; "donatable nitric oxide component"; "a free radical scavenging anti-oxidant molecule".

Furthermore, the use of the definition "analogue thereof" (claims 2 (part), 15 (part)) in the present context is considered to lead to a lack of clarity within the meaning of Article 6. The lack of clarity with respect to the functional claiming and ambiguous definitions is such as to render a meaningful complete search impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compound resveratrol as specified in examples 62-66 and claims 2 (part), 15 (part).

Continuation of Box No. III

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Claims 2 (part), 15 (part) are directed to the use of resveratrol in modulating transcription arising from an egr-1 response element consensus sequence.

Claims 2 (part), 15 (part) are directed to the use of 3, 4', 5 trinitroxy trans stilbene and 3, 4' tri(nitroxy)ethoxy trans stilbene in modulating transcription arising from an egr-1 response element consensus sequence.

*Claims 2 and 15 lack unity within the meaning of Rule 13.2 since the common concept linking together the resveratrol and 3, 4', 5 trinitroxy trans stilbene and 3, 4' tri(nitroxy)ethoxy trans stilbene is the trans stilbene core. Since the use of resveratrol in modulating transcription arising from an egr-1 response element consensus sequence is known, the trinitro(ethoxy) or trinitrooxy moieties are not a technical feature that define a contribution over the prior art.*

Claims 17-24 are directed to a method for identifying a compound capable of modulating expression of a gene associated with an egr-1 response element consensus sequence comprising AGCCCCGC and use of compounds identified by said method for the treatment of a disease or condition.

Claims 27-38 are directed to a flavonoid or isoflavonoid compound for modulating expression of a gene associated with an egr-1 response element, pharmaceutical compositions thereof, and use of the flavonoid or isoflavonoid compound in the manufacture of a medicament for the treatment of a disease or health condition associated with an expression state of a gene associated with an egr-1 response element consensus sequence.

Claims 39-44 are directed to a stilbene compound for modulating expression of a gene associated with an egr-1 response element, pharmaceutical composition thereof, and use of the stilbene or compound in the manufacture of a medicament for the treatment of a disease or health condition associated with an expression state of a gene associated with an egr-1 response element consensus sequence.

Claims 45-50 are directed to a chalcone compound for modulating expression of a gene associated with an egr-1 response element, pharmaceutical composition thereof, and use of the chalcone compound in the manufacture of a medicament for the treatment of a disease or health condition associated with an expression state of a gene associated with an egr-1 response element consensus sequence.

Claims 51-56 are directed to a polyphenol compound for modulating expression of a gene associated with an egr-1 response element, pharmaceutical composition thereof, and use of the polyphenol compound in the manufacture of a medicament for the treatment of a disease or health condition associated with an expression state of a gene associated with an egr-1 response element consensus sequence.

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/001818

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1. b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☐ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☒ furnished subsequently to this Authority for the purposes of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA2004/001818

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. ☐ Claims Nos. :  
because they relate to subject matter not required to be searched by this Authority; namely:
2. ☒ Claims Nos.: 1, 2 (part), 3-14, 15 (part), 16, 25-26  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :  
  
see PCT/ISA/210 (Extra Sheet)
3. ☐ Claims Nos. :  
because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule

## Box III Observation where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

see PCT/ISA/210 (Extra Sheet)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos. :
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos. : 2 (part), 15 (part)

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.